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BOSTON PROBES, INC.
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In re Application of	:	
Krishan L. Taneja	:	
Serial No.: 09/627,796	:	DECISION ON PETITION
Filed: 28 June	:	
Attorney Docket No.: BP9806US-CP2	:	

This letter is in response to the second renewed Petition under 37 C.F.R. 1.144 and 1.181, filed 25 October 2005, requesting reconsideration of the Petition Decision of 30 August 2005, denying the first Petition requesting withdrawal of the restriction requirement to a single set of peptide nucleic acid (PNA) probes.

BACKGROUND

A review of the file history shows that this application was filed on 28 July 2000 with 45 claims (64 pages) drawn to peptide nucleic acid probes and kits and methods for detecting, identifying or quantitating one or more human chromosomes.

A restriction requirement was mailed to applicant on 21 September 2001, requiring the restriction of the 45 claims in one of eighteen inventions under 35 U.S.C 121. The claims were restricted as follows:

Groups 1 - IV, VII, IX, and XVI, claims 1 - 15, 21 - 23, and 29 - 45, drawn to [peptide] nucleic acid probes directed to human chromosomes X, Y, 1, 2, 3, 6, 8, 10, 11, 12, 16, 17, and 18, respectively, and methods and kits for detecting, identifying, or quantitating said human chromosome in a sample, classified in class 536, subclass 23.1 and class 435, subclass 6;

Group VI, claims 1 - 16, 21 - 23, and 29 - 45, drawn to [peptide] nucleic acid probes directed to human chromosome 4 and methods and kits for detecting, identifying, or quantitating human chromosome 4 in a sample, classified in class 536, subclass 23.1 and class 435, subclass 6;

Group VIII, claims 1 - 15, 17, 21 - 23, and 29 - 45, drawn to [peptide] nucleic acid probes directed to human chromosome 7 and methods and kits for detecting,

identifying, or quantitating human chromosome 7 in a sample, classified in class 536, subclass 23.1 and class 435, subclass 6;

Group X, claims 1 - 15, 18, 21 - 23, and 29 - 45, drawn to [peptide] nucleic acid probes directed to human chromosome 9 and methods and kits for detecting, identifying, or quantitating human chromosome 9 in a sample, classified in class 536, subclass 23.1 and class 435, subclass 6;

Group XVII, claims 1 - 14, 19, 21 - 23, and 29 -45, drawn to [peptide] nucleic acid probes directed to human chromosome 20 and method and kits for detecting, identifying, or quantitating human chromosome 20 in a sample, classified in class 536, subclass 23.1 and class 435, subclass 6; and

Group XVIII, claims 1 - 15, 20 - 23, and 29 - 45, drawn to [peptide] nucleic acid probes directed to detecting, identifying, or quantitating human chromosome pair 13/21 in a sample, classified in class 536, subclass 23.1 and class 435, subclass 6.

The examiner stated that the reasons for the restriction was based upon the following reasons: Each group is directed to [peptide] nucleic acid sequences that identify or detect a different specific human chromosome. Each of the sequences are structurally and functionally different from each other. That is structurally, the sequences comprise a different sequence(s) of nucleobases, thus resulting in unique sequences. Functionally, the sequences are different in that they identify or detect different human chromosomes . . .

In response to the above restriction requirement applicant filed a response on 05 March 2002, electing with traverse Group II [peptide] nucleic acid probes, claims 1 - 15, 21 - 23 and 29 - 45, directed to kits and methods of detecting, identifying or quantitating human chromosome X (SEQ ID Nos. 10 - 16). However, no claim was presented which was limited to the elected invention.

On 21 April 2003 the examiner mailed to applicant a non-final Office action in which the restriction was made FINAL. Claims 16 - 20 and 24 - 28 were withdrawn from consideration as directed to a non-elected invention. Claims 1 - 15, 21 - 23, and 29 - 45 were rejected under 35 U.S.C. 112, first paragraph, for lack of an enabling disclosure and for lack of an adequate written description. Claims 1, 4 - 11, 13 - 15, 36 - 43, and 45 were rejected under 35 U.S.C. 102 over U.S. Patent 5,985,563.

On 29 January 2004 the examiner mailed to applicant a second non-final Office action in which claims 16 - 20 and 24 - 28 were also withdrawn as directed to a non-elected invention. Claims 2, 12, 38 and 34 were objected to. Claims 1, 3 - 11, 13 - 15, 21 - 23, and 29 - 45 continued to be rejected under 35 U.S.C. 112, first paragraph, for lacking an enabling disclosure and for lacking adequate written description. Claims 41 and 44 were rejected under 35 U.S.C. 112, second paragraph, for indefiniteness. Claims 10, 34,35, and 45 continued to be rejected under 35 U.S.C.102 over Hyldig-Neilsen (WO95/32305). Claims 1, 3 - 9, and 36 - 44 were rejected under 35 U.S.C. 103(a) as being obvious over Von Wintzingerolde et al. in view of Hyldig-Nielsen et al. (Ibid.).

On 03 August 2004 applicant filed a Petition under 37 C.F.R. 1.144 or 1.181 requesting withdrawal of the restriction requirement issued by the examiner on 21 September 2001.

On 12 April 2005 a Decision on the Petition filed 28 July 2004 denying applicant's request to withdraw the restriction requirement issued by the examiner on 21 September 2001.

On 27 April 2005 a third non-final rejection was mailed to applicant in which claims 16 - 20 and 24 - 28 as well as SEQ ID Nos. 1 - 9 and 18 - 159 were withdrawn as directed to a non-elected invention. Claims 1, 4 - 10, 13 - 15, 21, 29 - 33, 35 - 43, and 45, directed to chromosome Y probes (SEQ ID NOS 10 - 16) were under examination. Claims 10, 13 - 15, 21, 29 - 33, and 35 - 43 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Peptide nucleic acid (PNA) probes comprising a proving nucleobase sequence comprising SEQ ID NOS. 10 - 16 were searched and found to be free of the prior art. Furthermore, the examiner indicated that any claim drawn to a set of probes that contains at least one PCA probe comprising a probing nucleobase sequence selected from the group consisting of SEQ ID NOS 10 - 16 would also be free of the prior art. Finally, the examiner stated that if applicant intends that each set of probes contain at least 1 probe from each chromosome, as listed, the claims would no longer be objected to and would be allowable once the 112, second paragraph, issues were resolved, because each set would minimally comprise at least one PNA probe comprising probing nucleobase sequence selected from the group consisting of SEQ ID NOS. 10 - 16.

On 10 June 2005 applicant filed the first renewed petition under 37 C.F.R. 1.144 or 1.181 requesting reconsideration of the Decision on Petition mailed 12 April 2005 denying applicant's request for the withdrawal of the restriction requirement of 21 September 2001.

Applicants filed a response to the Office action on July 28, 2005, in which claims 10, 13, 16-21, 24-28, 35-36, 38 and 45 were amended and claim 43 canceled. The rejections and objections were also responded to.

On 30 August 2005 a Decision on Petition filed 10 June 2005 was mailed to applicant denying, again, applicant's request to withdraw the restriction requirement of 21 September 2001.

On October 17, 2005, the examiner mailed an Office action setting a one month period for reply indicating claims 10, 13-15, 35 and 45 as allowed and all other pending claims objected to as directed to non-elected subject matter and requesting their cancellation. No response has been made to this Office action as of the mailing of this decision.

On 25 October 2005 applicant filed yet a third petition requesting reconsideration of the Decision on Petition mailed 30 August 2005 denying applicant's request to

withdraw the restriction requirement of 21 September 2001. This is the petition now under consideration.

DISCUSSION

The application, file history and petition have been considered carefully.

Applicant maintains that the requirements deemed necessary by the Office to put the application in condition for allowance (and the Office's related refusal to consider Applicant's claims on their merits) conflict with applicant's right to claim his invention in the manner he deems appropriate under 35 U.S.C 112, first paragraph. Thus, it is believed that the restriction requirement and the related objection is improper and should be withdrawn.

Applicant supports his position by three central arguments.

(1) Applicant argues that the restriction controversy is resolved by proper application of *In re Weber*

Applicant argues that a proper application of *In re Weber, 580 F.2d.455, 198 USPQ 328 (CCPA)* would fully resolve the instant restriction requirement problem because Weber clearly teaches that any restriction within a single claim is improper since it prevents applicant from ever having the claim fully examined on the merits. Applicant further argues that the examiner should have required an election of species instead of a making a restriction requirement under 35 U.S.C. 121. Applicant emphasizes that just because a claim contains two or more inventions which are independent and distinct, a restriction requirement in lieu of an election of species is not justified. Finally, applicant asserts that the examiner is *de facto* rejecting the non-elected claims by requiring that the non-elected inventions be canceled, even though only formally objecting to them.

To support his argument that restriction within a single claim is improper, applicant points to the two citations from *In re Weber*:

> "It is apparent that § 121 provides the Commissioner with the authority to promulgate rules designed to Restrict an Application to one of several claimed inventions when those inventions are found to be "independent and distinct." It does not, however, provide a basis to an examiner acting under the authority of the Commissioner to Reject a particular Claim on that same basis."
> (In re Weber, 580 F.2d 455, 458, 198 U.S.P.Q. 328, 331-332 (CCPA, 1978))

> "We hold that a rejection under § 121 violates the basic right of the applicant to claim his invention as he chooses."
> (Weber at 459, 198 U.S.P.Q. at 332 (CCPA, 1978)

Applicant's argument has been fully considered but is not deemed persuasive.

The examiner is required to followed the interpretation of *In re Weber* provided by the M.P.E.P. 803.02:

Since the decisions In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F2d. 461, 198 USPQ334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ 2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (I) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

This subsection of the MPEP deals with Markush-like generic claims which include a plurality of alternately usable substances or members. In most cases, a recitation by enumeration is used because there is no appropriate or true generic language. A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claims with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, the examiner may require a provisional election of a single species prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability.

The Office agrees with applicant that in order to require an election of species within a Markush-type claim, more is required than simply the inventions being independent and distinct. The Office must show that it would be unduly burdensome to examine all the species if restriction were not required. Further, as indicated above in MPEP 803.02, the Office must additionally show that the inventions lack unity of invention, which requires the Office to establish that either there is a lack of common utility **or** a lack of a substantial structural feature essential to that common utility. Without these two requirements for unity of invention, i.e., common utility and substantial structural feature essential to that utility, there is nothing preventing an applicant from lumping into a single method of producing light claimed inventions as diverse as a flashlight, a carbon arc spotlight and a laser--all because they have the common utility of producing light. Clearly, a substantial structural feature in combination with a common utility is essential in defining any meaningful unity of invention. In the instant application claim 1 lacks both a substantial structural feature **and** a common utility with regard to the 159 SEQ ID NOS of the peptide nucleic acid probes, each possessing one of hundreds of thousands of peptide backbone variations.

A more detailed explanation in support of the lack of unity of invention in the instant invention is found in the section dealing with applicant's third central argument: that there exists a unity of invention among the claimed peptide nucleic acids.

(2) Applicant argues that the M.P.E.P. cannot cure the Office's faulty analysis

Applicant maintains that the Office's position of holding that applicants' claims (especially claim 1) are improper Markush claims because they lack unity of invention and are therefore subject to restriction under 35 U.S.C. 121 is unsound reasoning. Applicants' arguments have been fully considered but are not deemed persuasive.

The examiner analysis of the claims and the restriction requirement are not based upon some allegedly faulty analysis as indicated by the applicant. It is agreed that the examiner is required to follow the interpretation of case law as set forth in the M.P.E.P. Furthermore, it is clear from MPEP 803.02 from the Office's interpretation of *In re Weber* and other pertinent case law that an examiner is permitted to restrict within a claim under 35 U.S.C. 121 when the inventions encompassed by said claim lack unity of invention. Additionally, the M.P.E.P. clearly explains how claims directed to polynucleotide sequences claimed both individually and in sets will be restricted and examined. The instant claims recite both individual sequences (Example A: a method of using a probe comprising SEQ ID NO. 10), sets (Example B: method of using probes comprising using SEQ ID NOS. 10 – 16), and kits containing said probes, and methods of detecting, identifying, or quantitating specific human chromosomes X using one or more of the PNA probes.

MPEP 803.04 states that after restriction:

> Based upon the finding of allowable sequences, claims limited to allowable Sequences as in example A, all combinations, such as in examples (B) and (C), containing the allowable sequences and any patentably indistinct sequences will be rejoined and allowed.
>
> Rejoinder will be permitted for claims requiring any allowable sequence(s). Any claims which have been restricted and non-selected and which are limited to the allowable sequence(s) will be rejoined and examined.

At this point, because applicant has elected the PNA probes which requires all of SEQ ID NOS. 10 - 16 , and because the examiner has indicated this invention is free of the prior art and otherwise in condition for allowance, applicant must amend his claims to include at least one claim limited to the elected invention in order for the claim objections to be withdrawn and for a claim to be placed in condition for allowance. Applicant may also pursue generic linking claims which encompass all the features of the elected invention and should any of those become allowable, applicant may be entitled to rejoinder under MPEP 809 of any claims which require all the features of the allowable linking claim.

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[1] It is noted that the partial waiver of restriction for ten sequences discussed in 803.04 pertains only to product inventions comprising polynucleotide sequences and does not apply to process inventions, such as the method of using PNA probes.

For the instant invention, a linking claim could have been drafted in the format of claim 1 in which the list of alternative sequences in 1 was deleted.

Claims 10 - 16 and 24 - 28 are withdrawn to the extent that they read on method claims directed to individual SEQ ID NOS. 1 - 9 or 17 - 159 or to combinations other than the combination of all SEQ ID NOS. 10 - 16 pursuant to 37 CFR 1.142(b), Claims limited to a PNA probes of SEQ ID NOS. 10 - 16 will be allowed along with methods of using said probes for detecting human chromosome X. Additionally, upon indication of an allowable claim, applicants may include claims which require all the features of the allowable invention(s). At this time, no claim is in condition for allowance in view of the outstanding objection that all claims encompass non-elected subject matter.

3) Applicant maintains that "Unity of Invention" Exists

(a) Applicant holds that there is a substantial chemical structural feature among the SEQ ID NOs.

The claimed probes are not traditional nucleic acids. They are Peptide-Nucleic Acids (PNA) and have been claimed as "Non nucleic acid probes." The difference with a PNA is that the backbone is not a traditional sugar-phosphate nucleic acid backbone, but one that has peptide structures. PNA's function like nucleic acids in that they contain a sequence of bases (usually traditional nucleotide bases; termed in the claims as a probing nucleobase sequence) which is responsible for the hybridization of a PNA or DNA. Thus it is actually the nucleobase sequence that controls the function and specificity of these PNA's.

Claim 1 recites 159 sequences listed in the alternative. Representative SEQ ID NOS. 1 , 2, and 3 are shown below. No significant similarity is evidenced from a comparison of these three sequences. SEQ ID NOS 4 - 159 also appear to be unrelated, one to another, with respect to sequence similarity.

<400> 1
cttcaaagag gtccacga

<400> 2
agggttcaac tgtgtgac

<400> 3
gaaacttctg agtgatga

MPEP 2175.03(n) states in part that:

> When materials set forth in the Markush group ordinarily must belong to a recognized physical or chemical class or to an art recognized class. However, when the Markush group occurs in a claim reciting a process or a combination (not a single compound), it is sufficient if the members of the group are disclosed

> in the specification to possess at least one property in common which is mainly responsible for their function in the claimed relationship, and it is clear from their very nature or from the prior art that all of them possess this property.

For process and combination claims, the Markush group may include members which share a common property mainly responsible for their function in the claimed relationship. It is not clear from the comparison of SEQ ID NOS 1, 2, and 3, what property, if any, that they share which is mainly responsible for their function.

Moreover, on pages 21 - 24 of the specification, the Table illustrates that the probes are specific for different chromosomes. Thus, SEQ ID NO. 10 which may be used to detect chromosome Y would not be interchangeable with SEQ ID NO. 9 which may be used to detect chromosome X. The specification discloses that each probe 1 - 159 cannot be substituted one for another to obtain the same effect. The specification discloses that probes 153 - 159 are specific for two chromosomes 13/21; however, this invention was not elected for examination. Furthermore, it is not clear from the prior art or from their nature that all of the probes possess a property responsible for their function. For example, it is not clear what common sequence is shared by all SEQ ID NOS 10 - 16 that would impart the common substantial structural feature to all these sequences.

Applicants argue that the polypeptide backbone of the sequences is the substantial structural feature of the probes of SEQ ID NOs. 1 - 159 which provides the common utility of detection of human chromosomes This argument has been fully considered but is not deemed persuasive. The fact that the backbone of a nucleic acid or nucleic acid analog may vary so widely, e.g. from a polyanionic ribose phosphate backbone to a neutral polypeptide backbone emphasizes the lack of specificity of the backbone. The functionality (the hybridization to a complementary sequence) and specificity are provided by the sequence order of the four bases forming said backbone (ACTG). This is the property primarily responsible for their function in the claimed process of detecting of human chromosomes And as pointed out above in SEQ ID NOs. 1, 2, and 3, there is no apparent substantial structural feature, which is clear from their very nature or the prior art that is mainly responsible for their function in the claimed relationship in the sequences around which all of the SEQ ID NOs are grouped.

(3)(b) Applicants emphasize that there is a common utility shared by all of the SEQ ID NOs.

Applicant points to the examples in the specification to support their holding that the claimed probes have a common utility. From page 8 of the first renewed petition:

> That common utility was also demonstrated by the Examples and illustrated in the Figures. For Example, Figures 12A and 12B illustrate the simultaneous determination of chromosomes X, Y, and 1. Thus, it is remarkable that the Office could conclude that there is no common utility for these probes where the

specification clearly demonstrates the common utility.

The Brief description of the Drawnings for Figure 12 is set forth below.

> In Figure 12A and 12B the composite digital image was obtained with each of the blue, green, red (pseudo colored orange) and Cy5 (pseudo colored red) filters of a CCD camera attached to a microscope. Chromosomes X, Y, and 1 are clearly detectable in the visible interphase nuclei and metaphase spreads. The cells observed in Figure 12A are from a normal human female (XX,11) and the cells observed in Figure 12B are from a normal human male (XY, 11).

From the disclosure, it appears that 3 probes are used together to detect chromosome X, Y, and 11. A combination of probes specific for chromosome X, Y, and 11 are expected to detect a combination of chromosomes X, Y and 11, but this imparts a common utility among the three probes for X, Y, and 11. It is not clear whether applicant is arguing that an individual Probe for chromosome X would also specifically bind chromosome Y and 11. Table 1 does not disclose any individual probe which binds chromosomes X, Y, and 11.

MPEP 808 sets forth further guidance for insisting upon restriction:

> Every requirement to restrict has two aspects: (A) the reasons (as distinguished from the mere statement of conclusion) why the inventions *as claimed* are either independent or distinct; and (B) the reasons for insisting upon restriction there between as set forth in the following sections.

The arguments appear to be directed to the elected invention, probes comprising SEQ ID NOS 10 - 16. These arguments are not commensurate with the invention as claimed. MPEP 808 explains that it is the invention, as claimed, which is considered for distinctness or independence. It is noted that the invention as claimed does not require all SEQ ID NOS 10 - 16. Claim 1 encompasses individual probes and set of probes which do not require all SEQ ID NOS. 1 - 159. For these reasons, applicant's arguments that the probes do possess a common utility are not found persuasive.

It is clear that the critical issue in this restriction controversy is whether or not the inventions embraced by claim 1 in particular possess Unity of Invention. Applicant argues "Yes" and the Office disagrees. Since the Office has determined that Unity of Invention does not exist for claims involving sequences for the reasons noted above, it is reasonable and proper to apply 35 U.S.C. 121 to restrict the claimed inventions to a single group of SEQ ID NOS. used to identify a specific human chromosome.

Even though applicant has been required by the examiner to select a SINGLE combination of probes for examination of Group II, this is for examination purposes only. If during examination, the examiner finds that the nucleobase sequence of the any one of SEQ ID NOS. 10 - 16 is both novel and non-obvious, then the examiner would allow method claims directed to the use of those SEQ ID NOS.

In the 27 years since the CCPA decided *In re Weber*, there has been an explosion in molecular biology, genomics, and proteonomics which has created an entirely unforseeable search burden upon the Office. Even though initial sequence searching is done by computer, the examiner must review and analyze all of the references identified by the sequence search. The exponential increase in the size of the sequence data-bases created by the completion of the sequencing of the human (and other) genome has made the searching of more than a single SEQ ID No. an undue burden on the Office.

In conclusion, *In re Weber* is correct that applicants do have the right to have their entire claimed invention examined so long as there exists a Unity of Invention within that which is claimed. However, where Unity of Invention is lacking, it is proper to restrict the patentably distinct and independent inventions under 35 U.S.C. 121. This approach is a balance between the rights of the single instant inventor and the rights of other inventors to have their inventions examined in a timely manner.

DECISION

For the above reasons, this renewed petition to withdrawn the restriction requirement is **DENIED**.

Applicants remain under obligation to reply to the Office action mailed 17 October 2005 within the time period set therein or as extended under 37 CFR 1.136(a).

Any request for consideration of this decision must be filed within two (2) months of the mailing date of this decision in order to be considered timely.

Should there be any questions regarding this decision, please contact Special Program Examiner, William R. Dixon, Jr. by letter addressed to Director, TC 1600, at the address listed above, or by telephone at 571-272-0519 or by facsimile sent to the general Office facsimile number, 571-273-8300.

Jasemine C. Chambers
Director, Technology Center 1600